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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/733,179	12/07/2000	Heather A. Boux	12071-006001	3168
26161	7590	05/04/2004	EXAMINER	
FISH & RICHARDSON PC 225 FRANKLIN ST BOSTON, MA 02110			CHEU, CHANGHWA J	
			ART UNIT	PAPER NUMBER
			1641	

DATE MAILED: 05/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/733,179

Applicant(s)

BOUX ET AL.

Examiner

Jacob Cheu

Art Unit

1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19-32 and 35-54 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-32 and 35-54 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's amendment filed on 1/30/2004 has been received and entered into record and considered.

The following information provided in the amendment affects the instant application:

1. Claims 1-18, 33-34 have been cancelled.
2. Claims 36-54 are added to the instant application.
3. Currently, claims 19-32, 35-54 are under examination.

Claim Rejections - 35 USC § 112

Enablement

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
2. Claims 19-23, 26-31, 35-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), enablement requires that the specification teach those skilled in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The instant invention claims a “*specific* Hsp70B” monoclonal antibodies having characteristics against certain epitopes as recited in SEQ ID No. 1, 4, 6, 9 (or 8, See below §112, second paragraph rejection). However, applicant’s data do not support the notion that the isolated antibodies, particularly on the epitopes SEQ ID 1, 4 and 9, have the capability of differentiating Hsp70B’ among the Hsp70 families.

For residues 618-638, corresponding to SEQ ID No. 1, applicant fails to determine the cross-reactivity on Hsp70B. (See Table 4)

Residues 561-576, corresponding to SEQ ID 4, do not show its specificity for Hsp70B’ because it also against Hsc70 and Hsp70A. (See Table 4).

Residues 546-559, corresponding to SEQ ID 6, data indicates that there is cross-reactivity with Hsp70B. (See Table 4).

Similarly, residues 1-12, corresponding to SEQ ID 9 (or 8), do not show specificity because it reacts with Hsc70 and Hsp70A. (Table 4 designated as NT antibody) Furthermore, applicant *admits* that NT antibody has no utility in the differential detection of different Hsp70 family members. (See Table 4, page 43, last second paragraph)

With respect to the peptides recited as SEQ ID No. 7, 2, 3, 5, 10 for generating Hsp70B’ antibody also fall into the similar enablement problem.

With respect to SEQ ID No. 7, which is a fragment of SEQ ID No. 6, but there is no cross-reactivity data to show its specificity against any of the Hsp70 family proteins. (Table 4)

With respect to SEQ ID No. 2, corresponding to residues 624-618, fails to show data of cross-reactivity of DnaK and Hsp71. (See page 22, fourth paragraph, applicant *admits* that the above mentioned proteins are Hsp70 homolog, and were used to identify the specificity of the Hsp70B' antibody) Furthermore, for antibodies from rabbit and goat, there is no data to support cross-reactivity of Hsp70B. (Table 4) Similarly, SEQ ID No. 3, which shortens from SEQ ID No. 2 for only last 3 residues, shares the same problem.

With respect to SEQ ID No. 5, corresponding to residues 561-573, lacks data in support of cross-reactivity on Grp78, DnaK or Hsp71.

With respect to SEQ ID No. 10, corresponding to residues 553-567, no data support its specificity against Hsp70B.

Therefore, all the above antibodies lack the ability to specifically differentiate Hsp70B' from its Hsp70 family. In view of the aforementioned lack of predictability in the art, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in the applicant's specification of how to effectively practice the recited method and absent working examples.

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
2. Claims 19-32, 35-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 19, “Hsp70B” is vague and indefinite. It is unclear what are the metes and bounds of this Hsp70B’ protein. Particularly, applicant *clearly admits* that the instant invention used SEQ ID No. 11 as the Hsp 70B’ for the isolation antibody and detection purposes. (See amended specification, Figure 2, page 5, line 37, SEQ ID No. 11) One of the prior art, Leung et al. (Biochem. J. (1990) 267: 125), also uses the same Hsp 70B’ name, albeit with only 6 different amino acids in the whole 643 residues. (about 99% homology; See Sequence Comparison sent to Attorney Dr. Lee Crews by fax on April 29, 2004) Similarly, the rest of the claims share the same problem as in claim 19.

With respect to claim 22, line 7, “SEQ ID No. 9”, is confusing. Please check with SEQ ID No. 8 where the same amino acid residues are recited. Applicant needs to clarify.

With respect to claim 32, line 4, “a specific interaction” is vague and indefinite. It is suggested applicant use “binding” instead.

With respect to claims 42 and 43, the “KLH” should be spelled out completely.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
 3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
5. Claims 19-21, 32, 49, 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leung et al. over Campbell (Monoclonal Antibody Technology Campbell eds, 1986) in combination of Schild et al. (Curr Opinion in Immu. 1999 11: 109 February issue) or Srivastava et al. (US 6451316).

Leung et al. clone and sequence one of the heat shock protein family, Hsp 70B'. This Hsp 70B' protein has been associated with a variety of physiological regulations, particularly environmental stresses, such as heat or chemical substance, i.e. CdCl₂. (See Hsp 70B' sequence and page 131, right column, first paragraph) However, Leung et al. do not specifically teach making an antibody to detect Hsp70B' protein.

Two references, namely Schild et al. or Srivastava et al., have shown the antigenic natures in the Hsp70 family. (See Schild, Introduction and Abstract; Srivastava, Col. 5, line 60-65 and Section 5.4) Campbell teaches that "*it is customary now for any group working on a macromolecule to both clone the genes coding for it and make monoclonal antibodies to it (sometimes without a clear objective for their application)*". (See section 1.3.4 Basic Research) (emphasis added) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided Leung et al with basic technique for making antibody as taught by Campbell, since Hsp 70 family protein has been shown antigenic and involving important physiological functions, particularly environmental-stress response, one skilled in the art would be motivated to use Campbell's teaching to make monoclonal antibodies against Hsp 70B' with reasonable expectation of success once its sequence has been disclosed.

Response to Applicant's Arguments

6. The rejection of claims 19-21 and 32 as anticipated by Elthon et al. (US 6268548) under 35 USC §102 (b) is withdrawn.
7. The rejection of claims 22-31 as anticipated by Rosen et al. (US 20030064072) under 35 USC §102(a) is withdrawn.

With respect to obviousness rejections under Leung et al.

8. Applicant's arguments with respect to claims 19-21 have been considered but are moot in view of the new ground(s) of rejection.

The argument centered on that merely a single reference by Leung can not be prima facie sufficient to render the instant claims 19-21 obviousness. Particularly, applicant argues that Leung et al. do not specifically teach making any monoclonal antibodies to against Hsp70B'. Examiner has pointed out in this Office Action that the current invention shares about 99% homology with Leung et al., yet with the same name, Hsp70B'. The only different epitope might contributing to the difference in contrast to Leung et al. reference is the *whole* SEQ ID No. 9, (at residue 10, from Q to G, note the *first 9 residues epitopes* still fall within the Leung sequence). However, applicant had clearly admitted that this epitope can not serve a useful differential tool for specific Hsp70B' detection. (See above Enablement Rejection) The rest of the recited epitopes sequences are all within the exact sequence as revealed by Leung et al reference. (SEQ ID No. 1, 4, 6) As shown in the newly §103 rejection, it would be a prima facie obviousness for one skilled in the art to make an antibody against this Hsp70B'. (See above)

Allowable Subject Matter

9. Claims 24-25 are allowed.

Conclusion

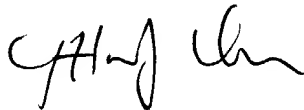
10. Claims 19-23, 2632, 35-54 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-282-0814. The examiner can normally be reached on 9:00-5:00.

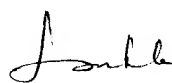
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jacob Cheu
Examiner
Art Unit 1641



April 29, 2003



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04/30/04